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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,743	05/09/2001	James Nolan	00-388-A	4067

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Kevin E. Noonan
McDonnell Boehnen Hulbert & Berghoff
32nd Floor
300 S. Wacker Drive
Chicago, IL 60606

EXAMINER	
SOROUSH, LAYLA	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
11/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/851,743	NOLAN ET AL.	
	Examiner	Art Unit	
	Layla Soroush	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-4,6-16,18-26,28-31 and 33-46* is/are pending in the application.

4a) Of the above claim(s) ~~8-12 and 24~~ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,13-16,18,19,25,26,28-31 and 33-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed August 8, 2007 presents remarks and arguments submitted to the office action mailed February 8, 2007 is acknowledged.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31,33-35, 36-46 over Banknieder et al US Patent 4,751,243 in view of York US Patent 4,600,717 and DiPiro et al Pharmacotherapy, A Pathophysiologic Approach, 2nd ed. Elsevier Pub, pp. 41-46 is not persuasive. Therefore, the rejection is maintained for reasons of record.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of Claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31,33-35, 36-46 over York US Patent 4,600,717 in view of FDA Guideline No. 38, Guideline For Effective Evaluation of Topical/Optic Animal Drugs, revised Aug 21, 1984, Center for Veterinary Medicine. 8/21/1984, available at. fda.gov/cvm/guidance/guidline38.htm. Last visited Sep 2005. ("Guideline No. 38"), Chen US Patent 6,232,341 and DiPiro et al Pharmacotherapy, A Pathophysiologic Approach, 2nd ed. Elsevier Pub, pp. 41-46 is not persuasive. Therefore, the rejection is maintained for reasons of record.

The rejection is restated below for applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31,33-35, 36-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banknieder et al US Patent 4,751,243 in view of York US Patent 4,600,717 and DiPiro et al Pharmacotherapy, A Pathophysiologic Approach, 2nd ed. Elsevier Pub, pp. 41-46.

The scope of the instant claims is viewed given their broadest reasonable interpretation consistent with the specification. Accordingly, the claims are directed to methods of identifying a compound for treatment of wounds to dermis or epidermis of external body surface in a diabetic animal, which also includes ophthalmic wounds. The method comprises producing a wound at a site of interest, expose the wound topically to an aldose reductase inhibitor, and assess the rate of wound healing. Claims 2 and 14 further require assessing the efficacy of another compound against the employed aldose reductase inhibitor.

Banknieder discloses methods of improving wound healing by administering an effective amount of tolerstat, which is an aldose reductase inhibitor compound to a patient. (abstract). Bankneider discloses methods of identifying the efficacy of tolerstat as a compound for healing wounds in diabetic rats against controlled subjects. (see col 2, line 13-col 3, line 20). Bankneider created a wound in diabetic animal models, treated the animals with controls, regular diet and tolerstat doses and subsequently determined that rats that were

treated with had improved wound healing (see entire col 2-3; claims 1-5). The wounds created by Bankneider is on the skin and thus on the dermis or epidermis of the subjects. The controls and regular diet of Bankneider's Group III meets the limitations of the instant claim 2 and 14 of comparing wounds in the presence of a test compound, because at least the instantly recited test compounds encompass the regular diet of Bankneider. Bankneider further claims methods of treating human with wounds from diabetes mellitus. Bankneider only fails to administer his aldose reductase inhibitor topically the epidermis or dermis wound and use punch biopsy to produce the wound.

York shows topical administration of aldose reductase inhibitors in suitable carrier system. York also shows effective treatment of ocular wounds in humans administering various aldose reductase inhibitors also disclosed in his parent cases. (see abstract, col 1, lines 25-59; col 2, lines 1-67).

Depiro et al is merely used to show that it is well within the purview of one of ordinary skill in the art to prepare a topical or ophthalmic formulation, once in possession of the active ingredient. (see p 42-45, specifically sections under biopharmaceutical and therapeutic considerations). Accordingly, converting a ophthalmic to a topical composition is a matter of optimizing the carrier system.

Thus, it would have been also obvious to one of ordinary skill in the art at the time of invention to practice Banknieder's method by administering his aldose reductase inhibitor topically to a site of interest on the skin, because as shown by York, such compounds as aldose reductase inhibitors, can provide their wound healing properties when administered topically. The ordinary skill in the art would

have had a reasonable expectation of success because, as described by York, aldose reductase inhibitors provide their wound healing effects when administered topically.

In addition, absence of a showing unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to treat a wound in respective studied subjects by any known mechanism of producing a wound, such as punch biopsy, because the ordinary skill in the art would have expected to see the samq results in any type of skin wound created on the skin.

The limitation of measuring the wound size is envisaged by a skilled artisan, because a parameter is needed in order to compare resulting wound healing.

Claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31,33-35, 36-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over York US Patent 4,600,717 in view of FDA Guideline No. 38, Guideline For Effective Evaluation of Topical/Optic Animal Drugs, revised Aug 21, 1984, Center for Veterinary Medicine. 8/21/1984, available at. fda.gov/cvm/guidance/guidline38.htm. Last visited Sep 2005. ("Guideline No. 38"), Chen US Patent 6,232,341 and DiPiro et al Pharmacotherapy, A Pathophysiologic Approach, 2nd ed. Elsevier Pub, pp. 41-46.

York shows topical administration of aldose reductase inhibitors in suitable carrier system. (abstract, col 2, lines 30-65). York also shows suggests effective treatment of ocular wounds in diabetic humans by administering various aldose reductase inhibitors. (see abstract, col 1, lines 20-59; col 2, lines 1-67). York fails

to compare the efficacy of his compositions against other potentially useful agents.

Guideline No. 38 is merely used to show the standard for assessing topical efficacy of candidate drugs. Attention is drawn to section VIII-X, wherein the study format and appropriate control groups are recommended by the FDA to substantiate the efficacy results of any give drug. (see specifically Sec IX).

Chen is used as an example of the Guideline No. 38 in a clinical efficacy study. Chen shows the state of art as to methods of assessing the efficacy of topical therapeutic preparation in treating skin wound comprising creating a wound, applying the drug of interest randomly among animals, comparing the rate of healing and assessing the efficacy of the drug (see example 3, col 5-8). Chen does not teach the use of his methodology on comparing the efficacy of topical agents against aldose reductase inhibitors in diabetic animals.

Depiro et al is merely used to show that it is well within the purview of one of ordinary skill in the art to prepare a topical or ophthalmic formulation, once in possession of the active ingredient. (see p 42-45, specifically sections under biopharmaceutical and therapeutic considerations). Accordingly, converting a ophthalmic to a topical composition is a matter of optimizing the carrier system.

Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of invention, to use compare aldose reductase inhibitors of York against other potential candidate agents by as described by Guideline No. 38 and exemplified by Chen's methodologies, because as taught by the Guideline No. 38 and Chen, such methods of comparative analysis is well practiced in the

art for assessing the cutanaous effects of drugs on ulcer or burn wounds of dermis or epidermis. The ordinary artisan would have had a reasonable expectation in observing positive results comparative results against aldose reductase inhibitors because they are proven to be effective as a wound-healing agent.

The limitation of measuring the wound size is envisaged by a skilled artisan, because a parameter is needed in order to compare resulting wound healing.

Response to Arguments

Applicant's arguments filed August 8, 2007 have been fully considered but they are not persuasive for the reasons set forth below.

Applicant argues that they have limited their claims to wounds to the dermis/epidermis, terms the skilled worker would understand do not encompass ophthalmic injuries. However, Examiner respectfully states Bankneider created a wound in diabetic animal models, treated the animals with controls, regular diet and tolerstat doses and subsequently determined that rats that were treated with had improved wound healing (see entire col 2-3; claims 1-5). The wounds created by Bankneider is on the skin and thus on the dermis or epidermis of the subjects. Accordingly, the limitation of treating wounds to the dermis/epidermis is met by the prior art reference. Therefore, Applicant's arguments are not found persuasive.

Additionally, in response to Applicants argument that the method of identifying an aldose reductase inhibitor for topical administration to facilitate wound healing in a diabetic animal was not obvious in light of systemic use of ARI is not persuasive. Examiner points to York where the equivalence of topical and systemic delivery is taught. More specifically, York teaches in the background of the invention "these aldose reductase inhibitors can be applied topically to the eye or systemically to the diabetic to promote wound healing when indicated (col. 1 lines 35-40)." Examiner also, respectfully reiterates that York shows aldose reductase inhibitors are also suitable and effective in treatment through carrier systems appropriate for topical and ocular administration in humans. (see abstract, col 1, lines 25-59; col 2, lines 1-67).

Applicant argues that the skilled artisan would not have been motivated to consider the cited art directed to aldose reductase inhibitor compounds (ARIs) known and used for systemic administration for treating wounds or ophthalmic injuries for treating wounds topically; specifically, this art would not have motivated the skilled worker to treat skin wounds created by punch biopsy to be measured by rate intervals of wound healing. Examiner reiterates the York reference teaches the equivalence of topical and systemic delivery. Further, Depiro et al. is used to show that it is well within the purview of one of ordinary skill in the art to prepare a topical or ophthalmic formulation, once in possession of the active ingredient. (see p 42-45, specifically sections under biopharmaceutical and therapeutic considerations). Accordingly, converting a ophthalmic to a topical composition is a matter of optimizing the carrier system.

Thus, it would have been also obvious to one of ordinary skill in the art at the time of invention to practice Banknieder's method by administering his aldose reductase inhibitor topically to a site of interest on the skin, because as shown by York, such compounds as aldose reductase inhibitors, can provide their wound healing properties when administered topically. The ordinary skill in the art would have had a reasonable expectation of success because, as described by York, aldose reductase inhibitors provide their wound healing effects when administered topically.

Applicant argues that the reference is also devoid of any teaching related to punch biopsy to produce a wound. It is the Examiners position that the mechanism of producing a wound is irrelevant to the actual invention -- "a method of identifying a compound that improves treatment of wounds to dermis or epidermis in a diabetic animal." Additionally, it would have been obvious to one of ordinary skill in the art at the time of invention to treat a wound in respective studied subjects by any known mechanism of producing a wound, such as punch biopsy, because the ordinary skill in the art would have expected to see the same results in any type of skin wound created on the skin.

In response, to Applicants argument that the pending claim set does not contain any claims relating to the subject matter of the DiPiro reference, Examiner draws Applicants attention to the rejection above wherein the DiPiro reference is merely used to show that it is well within the purview of one of ordinary skill in the art to prepare a topical or ophthalmic formulation, once in possession of the active ingredient. (see p 42-45, specifically sections under

biopharmaceutical and therapeutic considerations). Therefore, converting the topical ocular composition of York into a topical epidermal composition is a matter of optimizing the carrier system. Hence, Applicant's argument regarding the DiPiro reference is not persuasive.

Applicant argues "the Chen reference, cited in support of the asserted obviousness rejection, in fact teaches that what can be expected in instances of topical administration of drugs or drug lead compounds include that they are found to "both irritating and toxic" and "may result in contact dermatitis" or "are found to make some complications (such as fungal infections) worse." Chen, pg. 1, Background of the Invention. These teachings include a wide variety of compounds to be tested for topical administration, including anti-bacterial agents, antibiotics, and compound preparations with corticosteroids - all of which have diverse chemical formulae and properties. Thus, the art teaches that topical administration is in fact unpredictable. " However, Examiner states that the Chen reference is solely incorporated to show the instant claimed method steps are known to have been used in assessment of other compounds. Chen's assertion that certain anti-bacterial agents and corticosteroids by themselves cause irritation and toxic is irrelevant because the method steps as claimed are used for both positive and negative outcomes.

The arguments are not persuasive and the rejection is made **FINAL**.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER